J&J-106US Appln. No.: 10/766,631

Amendment Dated January 5, 2007

Reply to Office Action of October 19, 2006

Amendments to the Claims: This listing of claims will replace all prior versions, and listings,

of claims in the application.

Listing of Claims:

(Currently Amended) An aqueous formulation comprising consisting essentially 1.

of, on a gram per 100 ml (w/v) (reported as %) basis:

1-2 % 2,6-diisopropylphenol;

water; and up to 15% excipients, wherein said excipients consist consisting essentially

of, on a gram per ml total formulation basis, up to 6% polyethylene glycol (PEG), up to 10% of

a block copolymer, namely poloxamer 188, and optionally, one or more pH modifiers,

stabilizers, or tonicity modifiers, and wherein said formulation comprising is an aqueous

solution clear to the naked eye.

2-9. (Canceled)

10. (Canceled)

11. (Currently Amended) The formulation of claim 1, wherein the total amount of

said block copolymer is from-about 5% to about-10%-(w/v) of said formulation.

12. (Currently Amended) The formulation of claim 1, wherein the total amount of

said block copolymer is from about 6% to 8%-(w/v) of said formulation.

13. (Canceled)

14. (Canceled)

15. (Canceled)

16. (Canceled)

(Canceled) 17.

(Canceled) 18.

Amendment Dated January 5, 2007

Reply to Office Action of October 19, 2006

19. (Canceled)

20. (Currently Amended) The formulation of claim 1, wherein the amount of 2,6-

diisopropylphenol is about 1%-(w/v) of said formulation.

21. (Canceled)

22. (Canceled)

23. (Currently Amended) The formulation of claim 1, wherein the total amount of

PEG is less than about 5% (w/v) of said formulation.

24. (Currently Amended) The formulation of claim 1, wherein the total amount of

PEG is between about 2% and about-6%-(w/v) of said formulation.

25. (Previously Presented) The formulation of claim 24 wherein the PEG is between

about 2% and 4% of said formulation.

26. (Currently Amended) The formulation of claim 1, wherein the total amount of

PEG is between about 3 and 4%-(w/v) of said formulation.

27. (Previously Presented) The formulation of claim 1, wherein said PEG is selected

from the group consisting of PEG-300, PEG-400, PEG-600, PEG-800, and PEG-1000.

28. (Previously Presented) The formulation of claim 27, wherein said PEG is PEG-

400.

29. (Currently Amended) The formulation of claim 1, wherein said excipients include

propylene glycol and said propylene glycol is not more than 5%-(w/v) of said formulation.

30. (Currently Amended) The formulation of claim 29, wherein the amount of

propylene glycol is not more than 2% - (w/v) of said formulation.

31. (Currently Amended) The formulation of claim 30, wherein the amount of

propylene glycol is 1% or to 2% - (w/v) of said formulation.

32. (Previously Presented) The formulation of claim 1, wherein said excipients

include citric acid or a salt thereof.

Amendment Dated January 5, 2007

Reply to Office Action of October 19, 2006

33. (Currently Amended) The formulation of claim 32, wherein the concentration of said citric acid in said formulation is in the range of from 2.5 to 15 mM.

34. (Previously Presented) The formulation of claim 32, wherein said formulation

comprises citric acid in an amount of about 2 mg/ml.

35. (Previously Presented) The formulation of claim 1, wherein said excipients

include an antimicrobial agent.

36. (Currently Amended) The formulation of claim 35, wherein said antimicrobial

agent is selected from the group consisting of disodium edetate, metabisulfate, benzyl alcohol,

cysteine or a salt thereof, and EDTA.

37. (Currently Amended) The formulation of claim 36, wherein said antimicrobial

agent is benzyl alcohol in the amount of up to 0.5% - (w/v) of said formulation.

38. (Canceled)

39. (Currently Amended) The formulation of claim 28, wherein poloxamer 188 is

present in an amount between 6 and 8%—(w/v) of said formulation; PEG-400 is present in an

amount between 2 and 4%-(w/v) of said formulation; and the excipients include propylene

glycol in an amount not greater than 2% - (w/v) of said formulation.

40. (Currently Amended) The formulation of claim 28, wherein poloxamer 188 is

present in an amount of about 8%-(w/v) of said formulation; PEG-400 is present in an amount

of about 4%-(w/v) of said formulation; propylene glycol is present as an excipient in an amount

of about 1%-(w/v) of said formulation; and 2,6-diisopropylphenol is present in an amount of

about 1% (w/v) of said formulation.

41. (Currently Amended) The formulation of claim 28, wherein poloxamer 188 is

present in an amount of about 8%-(w/v) of said formulation; PEG-400 is present in an amount

of about 3%-(w/v) of said formulation; propylene glycol is present as an excipient and in an

amount of about 1%-(w/v) of said formulation; and 2,6-diisopropylphenol is present in an

amount of about 1% - (w/v) of said formulation.

42. (Currently Amended) The formulation of claim 28, wherein poloxamer 188 is

present in an amount of about 7%-(w/v) of said formulation; PEG-400 is present in an amount

Page 5 of 22

Amendment Dated January 5, 2007

Reply to Office Action of October 19, 2006

of about 4% - (w/v) of said formulation; propylene glycol is present as an excipient in an amount of about 1% - (w/v) of said formulation; and 2,6-diisopropylphenol is present in an amount of about 1% - (w/v) of said formulation.

43. (Currently Amended) The formulation of claim 28, wherein poloxamer 188 is present in an amount of about 7%–(w/v) of said formulation; PEG-400 is present in an amount of about 3%–(w/v) of said formulation; propylene glycol is present, as an excipient, in an amount of about 1%–(w/v) of said formulation; and 2,6-diisopropylphenol is present in an amount of about 1%–(w/v) of said formulation.

- 44. (Currently Amended) The formulation of claim 28, wherein poloxamer 188 is present in an amount of about 6%—(w/v) of said formulation; PEG-400 is present in an amount of about 4%—(w/v) of said formulation; propylene glycol is present, as an excipient, in an amount of about 1%—(w/v) of said formulation; and 2,6-diisopropylphenol is present in an amount of about 1%—(w/v) of said formulation.
- 45. (Currently Amended) The formulation of claim 28, wherein poloxamer 188 is present in an amount of about 6%—(w/v) of said formulation; PEG-400 is present in an amount of about 4%—(w/v) of said formulation; propylene glycol is present, as an excipient, in an amount of about 2%—(w/v) of said formulation; and 2,6-diisopropylphenol is present in an amount of about 1%—(w/v) of said formulation.
- 46. (Currently Amended) The formulation of claim 28, wherein poloxamer 188 is present in an amount of about 6%—(w/v) of said formulation; PEG-400 is present in an amount of about 6%—(w/v) of said formulation; propylene glycol is present, as an excipient, in an amount of about 1%—(w/v) of said formulation; and 2,6-diisopropylphenol is present in an amount of about 1%—(w/v) of said formulation.
- 47. (Currently Amended) The formulation of claim 28, wherein poloxamer 188 is present in an amount of about 8%—(w/v) of said formulation; PEG-400 is present in an amount of about 2%—(w/v) of said formulation; propylene glycol is present, as an excipient, in an amount of about 1%—(w/v) of said formulation; and 2,6-diisopropylphenol is present in an amount of about 1%—(w/v) of said formulation.
- 48. (Currently Amended) The formulation of claim 28, wherein poloxamer 188 is present in an amount of about 7%-(w/v) of said formulation; PEG-400 is present in an amount

Amendment Dated January 5, 2007

Reply to Office Action of October 19, 2006

of about 2%—(w/v) of said formulation; propylene glycol is present, as an excipient, in an amount of about 1%—(w/v) of said formulation; and 2,6-diisopropylphenol is present in an amount of about 1%—(w/v) of said formulation.

49. (Currently Amended) An aqueous formulation, comprising consisting essentially of, on a gram per 100 ml (hereafter %) total formulation basis:

- a. 2,6-diisopropylphenol; and
- b. water, and
- c. up to 15%—(w/v) excipients, wherein said excipients comprising—consist essentially of poloxamer 188 a block copolymer in an amount of less than about 10% (w/v) of said formulation, a polyethylene glycol in an amount of between about 2% and 4% (w/v) of said formulation, and optionally, one or more pH modifiers, stabilizers, or tonicity modifiers, and wherein the formulation includes no other glycol or alcohol and is transparent clear to the naked eye.
- 50. (Currently Amended) The formulation of claim 49, wherein said block copolymer poloxamer 188 is present in an amount of between about 5% to about 9% (w/v) of said formulation; and said polyethylene glycol is PEG-400, present in an amount of between about 2% and 4% (w/v) of said formulation.
- 51. (Currently Amended) The formulation of claim 50, wherein <u>said</u> poloxamer 188 is present in an amount of about 8% (w/v) of said formulation; PEG-400 is present in an amount of about 4% (w/v) of said formulation; and 2,6-diisopropylphenol in an amount of about 1% (w/v) of said formulation, wherein said formulation is substantially free of propylene glycol.
- 52. (Currently Amended) The formulation of claim 50, wherein <u>said</u> poloxamer 188 is present in an amount of about 8%—(w/v) of said formulation; PEG-400 is present in an amount of about 3% (w/v) of said formulation; and 2,6-diisopropylphenol is present in an amount of about 1%—(w/v) of said formulation, wherein said formulation is substantially free of propylene glycol.
- 53. (Currently Amended) The formulation of claim 50, wherein <u>said</u> poloxamer 188 is present in an amount of about 7% (w/v) of said formulation; PEG-400 is present in an amount

J&J-106US

Appln. No.: 10/766,631

Amendment Dated January 5, 2007

Reply to Office Action of October 19, 2006

of about 4%  $\frac{(w/v)}{(w/v)}$  of said formulation; and 2,6-diisopropylphenol is present in an amount of about 1%  $\frac{(w/v)}{(w/v)}$  of said formulation, wherein said formulation is substantially free of propylene glycol.

- 54. (Currently Amended) The formulation of claim 50, wherein <u>said</u> poloxamer 188 is present in an amount of about 7% (w/v) of said formulation; PEG-400 is present in an amount of about 3% (w/v) of said formulation; and 2,6-diisopropylphenol is present in an amount of about 1% (w/v) of said formulation, wherein said formulation is substantially free of propylene glycol.
- 55. (Currently Amended) The formulation of claim 50, wherein <u>said</u> poloxamer 188 is present in an amount of about 9% (w/v) of said formulation; PEG-400 is present in an amount of about 2% (w/v) of said formulation; and 2,6-diisopropylphenol is present in an amount of about 1% (w/v) of said formulation.
- 56. (Currently Amended) The formulation of claim 50, wherein <u>said</u> poloxamer 188 is present in an amount of 8% (w/v) of said formulation; and PEG-400 is present in an amount of 2% (w/v) of said formulation.
- 57. (Currently Amended) The formulation of claim 50, wherein <u>said</u> poloxamer 188 is present in an amount of 7% (w/v) of said formulation; and PEG-400 is present in an amount of 2% (w/v) of said formulation.
- 58. (Previously Presented) The formulation of claim 49, further comprising, in the excipient portion thereof, citric acid or a salt thereof.
- 59. (Currently Amended) The formulation of claim 58, wherein said formulation comprises citric acid is at a concentration between about 2.5 and 10 mM.
- 60. (Previously Presented) The formulation of claim 49, further comprising, in the excipient portion thereof, an antimicrobial agent.
- 61. (Previously Presented) The formulation of claim 60, where said antimicrobial agent is benzyl alcohol.
- 62. (Previously Presented) The formulation of claim 1 or claim 49, wherein said formulation further comprises, in the excipient portion thereof, polysorbate.

Amendment Dated January 5, 2007

Reply to Office Action of October 19, 2006

63. (Currently Amended) The formulation of claim 62, further including in the excipient portion thereof, polyoxyethylene 20 sorbitan monooleate in an amount of about 0.5 to about 15 percent  $\frac{(w/v)}{v}$  of said formulation; propylene glycol in an amount of about 0.5 to about 15 percent  $\frac{(w/v)}{v}$  of said formulation; PEG-400 in an amount of about 1 to about 20 percent  $\frac{(w/v)}{v}$  of said formulation; and poloxamer 188 in an amount of about 2 to about 15 percent  $\frac{(w/v)}{v}$  of said formulation.

64. (Currently Amended) The composition of claim 1 or claim 49, wherein said block copolymer poloxamer 188 is purified poloxamer 188, wherein said purified poloxamer has a polydispersity value of between about 5 and 1, about 4 and 1, about 3 and 1, about 2 and 1, or about 1.1 and 1.

65. (Canceled)

66. (Currently Amended) An aqueous formulation, consisting essentially of, on a gram per 100 ml (reported as %) total formulation basis:

a. a block copolymer in an amount of less than about 10%  $\frac{(w/v)}{(w/v)}$  of said formulation;

b. a polyethylene glycol in an amount of between about 2% and  $\frac{1}{2}$  and  $\frac{1}{2}$  of said formulation;

- c. 2,6-diisopropylphenol;
- d. water;
- e. optionally citric acid or a salt thereof; and
- f. optionally an antimicrobial agent

said components a, b, e, and f comprising excipients of said formulation, said excipients, in total, not exceeding 15% (w/v) of said formulation, said formulation being clear to the naked eye.

67. (Previously Presented) The formulation of claim 66, wherein said citric acid or a salt thereof comprises citric acid.

Appln. No.: 10/766,631

Amendment Dated January 5, 2007

Reply to Office Action of October 19, 2006

68. (Previously Presented) The formulation of claim 66, wherein the excipients of said formulation include an antimicrobial agent.

- 69. (Canceled)
- 70. (Canceled)
- 71. (Currently Amended) A microemulsion, consisting essentially of:
  - a block copolymer, namely poloxamer 188;
  - b. a polyethylene glycol (PEG);
  - c. 2,6-diisopropylphenol;
  - d. propylene glycol; and
  - e. water,

said components a, b, and d comprising excipients and said excipients not exceeding 15% grams per 100 ml (w/v) of said formulation, said microemulsion being lipid-free and clear to the naked eye.

- 72. (Currently Amended) An aqueous formulation, consisting essentially of <u>(on a weight/volume grams/100 ml % basis)</u>:
- a. a block copolymer, namely poloxamer 188 in an amount of less than about 10%  $\frac{(w/v)}{(w/v)}$  of said formulation;
- b. a polyethylene glycol in an amount of between about 2% and 4%  $\frac{(w/v)}{(w/v)}$  of said formulation;
  - c. 2,6-diisopropylphenol; and
  - d. water;

said components a and b comprising no more than 15% (w/v) of said formulation, wherein said formulation has an average particle size of less than about 65 nanometers.

Amendment Dated January 5, 2007

Peoply to Office Action of October 19, 2

Reply to Office Action of October 19, 2006

73. (Previously Presented) A method of inducing or maintaining anesthesia in a mammal, comprising administering to said mammal an amount of a formulation, as claimed in any one of claims 1, 49, 75 or 66, effective to induce or maintain anesthesia.

- 74. (Previously Presented) A multi-use container, comprising the formulation as claimed in any one of claims 1, 49, 66, or 75.
- 75. (Currently Amended) A formulation comprising a injectable anesthetic solution, including citric acid and an antimicrobial agent as optional components, said formulation including no more than 15% (weight/volume grams/100 ml) excipients and consisting essentially of, in addition to said optional components, a clear aqueous composition selected from the group consisting of:
  - a. 1% propofol, 9% poloxamer 188, 2% PEG 400, and water;
  - b. 1% propofol, 8% poloxamer 188, 4% PEG 400, and water;
  - c. 1% propofol, 8% poloxamer 188, 4% PEG 400, 1% propylene glycol, and water;
  - d. 1% propofol, 8% poloxamer 188, 3% PEG 400, and water;
  - e. 1% propofol, 8% poloxamer 188, 3% PEG 400, 1% propylene glycol, and water;
  - f. 1% propofol, 7% poloxamer 188, 4% PEG 400, and water; and
  - g. 1% propofol, 7% poloxamer 188, 4% PEG 400, 1% propylene glycol, and water.
- 76. (Previously Presented) The formulation of claims 1 or 49 wherein said pH modifiers are selected from the group consisting of sodium hydroxide, potassium hydroxide, and hydrochloric acid.
  - 77. (Currently Amended) An aqueous formulation consisting essentially of:
  - a. 2,6-diisopropylphenol; and
  - b. water; and

Amendment Dated January 5, 2007

Reply to Office Action of October 19, 2006

c. up to 15% excipients, wherein said excipients consist essentially of, on a gram per 100 mL total formulation basis, 8% poloxamer 188, 3% polyethylene glycol 400, 1% propylene glycol, 0.2% citric acid monohydrate, a preservative, and sodium hydroxide, and wherein said formulation is clear to the naked eye.

78. (Currently Amended) The formulation of any of claims 1, 49, 66, 71, 75, or <u>77</u> having an average particle size of from about 30 to <del>about</del> 75 nanometers.